

WHAT IS CLAIMED IS:

1 1. An apparatus comprising:
 2 a) a carousel that is rotatable around an axis, the carousel
 3 comprising a plurality of reaction mounts, each reaction mount comprising at least one
 4 reaction well arranged on a radius with respect to the axis, the radii spaced apart at equal
 5 angles, whereby the wells are arranged in at least one concentric circle around the axis;
 6 b) a rotator that rotates the carousel step-wise around the axis, each
 7 incremental step docking each of the reaction mounts at a separate station;
 8 c) a fluid delivery system that delivers liquid to at least one
 9 reaction well in each of a plurality of docked reaction mounts;
 10 d) a drain system that drains liquid by differential pressure from at
 11 least one reaction well of each of a plurality of docked reaction mounts; and
 12 e) a programmable digital computer that controls the rotator, the
 13 fluid delivery system and the drain system.

1 2. The apparatus of claim 1 wherein:
 2 (i) each reaction well comprises a drainage hole;
 3 (ii) the carousel comprises a plate which comprises a
 4 plurality of liquid conduits that connect with the drainage holes and are engagable with
 5 the drain system; and
 6 (iii) the drain system is a vacuum drain system comprising:
 7 (1) a plurality of vacuum lines that connect with
 8 vacuum source and
 9 (2) conduit engagement means that engage the
 10 vacuum lines with a plurality of the liquid conduits when the reaction mounts are docked
 11 at a station, whereby liquid in the reaction wells is drained through the vacuum lines.

1 3. The apparatus of claim 2 wherein:
 2 (i) each liquid conduit comprises:
 3 (1) a depression in the plate below the reaction
 4 mount which forms a chamber with the reaction mount, wherein the chamber
 5 communicates with the drainage holes of the reaction mount;
 6 (2) an exit port exiting under the plate; and

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- 7 (3) a bore through the plate the connects the
8 chamber with the exit port; and
9 (ii) the conduit engagement means comprises:
10 (1) a non-rotating connector plate positioned under
11 the carousel; the connector plate having an engagement port that is engagable with the
12 exit port positioned at each station, wherein each of a plurality of the engagement ports is
13 connected to a vacuum line; and
14 (2) an actuator that raises the connector plate to
15 engage the plurality of engagement ports with the plurality of exit ports.

- 1 4. The apparatus of claim 2 wherein the fluid delivery system
2 comprises:
3 (i) an assembly positioned above the carousel, the assembly
4 comprising a plurality of dispensing modules mounted at each of a plurality of the
5 stations, each dispensing module comprising a dispensing head adapted to deliver fluid to
6 the well of a reaction mount docked at the station;
7 (ii) a plurality of fluid dispensers, each dispenser adapted to
8 dispense an amount of fluid;
9 (iii) a plurality of fluid lines, each fluid line connecting a
10 fluid dispenser to a dispensing head.

- 1 5. The apparatus of claim 2 wherein the number of reaction mounts
2 equals the number of stations.

- 1 6. The apparatus of claim 2 wherein the carousel comprises 24
2 reaction mounts.

- 1 7. The apparatus of claim 2 wherein the reaction mounts each
2 comprise 8 reaction wells.

- 1 8. The apparatus of claim 2 wherein the fluid delivery system delivers
2 liquid to at least one reaction well in each of at least 3 docked reaction mounts and the
3 vacuum drain system drains liquid from at least one reaction well of each of at least 3
4 docked reaction mounts.

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1 9. The apparatus of claim 2 further comprising a temperature
2 controlling system that regulates the temperature of at least one reaction mount docked at
3 a station.

1 10. The apparatus of claim 2 further comprising an optical analyzing
2 system that optically analyzes fluid in a well of at least one reaction mount docked at a
3 station.

1 11. The apparatus of claim 4 wherein:
2 (i) each reaction mount comprises a plurality of wells;
3 (ii) each dispensing module comprises a motor that moves
4 the dispensing head to positions suitable for delivering fluid to each of the plurality of
5 wells.

1 12. The apparatus of claim 4 wherein at least one station comprises
2 both a dispensing module and an engagement port connected to a vacuum line.

1 13. The apparatus of claim 4 wherein each reaction mount comprises a
2 plurality of wells; the wells being spaced apart about the distance of wells in a row of a
3 96-well microtiter plate.

1 14. The apparatus of claim 4 further comprising an airtight chamber
2 that comprises the rotator, the dispensing assembly, the carousel and the connector plate.

1 15. The apparatus of claim 11 wherein at least one dispensing head is
2 connected to a plurality of fluid dispensers by fluid lines.

1 16. The apparatus of claim 14 wherein the chamber comprises an upper
2 chamber and a lower chamber wherein the upper chamber comprises the rotator and the
3 dispensing assembly, and the lower chamber comprises the carousel and the connector
4 plate, and wherein the lower chamber can be in a raised or lowered position with respect
5 to the upper chamber, and wherein in the raised position, the chamber forms an airtight
6 seal.

1 17. The apparatus of claim 14 comprising a regulator which regulates a
2 directional flow of a gas to the upper chamber.

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1 18. The apparatus of claim 16 further comprising a bellows connected
2 to the regulator and to the upper chamber which functions as a reservoir for the gas.

1 19. A method for performing in parallel a series of physical steps in a
2 chemical reaction protocol, wherein the protocol generates a chemical linkage in a parent
3 molecule, the method comprising:

4 a) providing a carousel that is rotatable around an axis, the carousel
5 comprising a plurality of reaction mounts, each reaction mount comprising at least one
6 reaction well arranged on a radius with respect to the axis, the radii spaced apart at equal
7 angles, whereby the wells are arranged in at least one concentric circle around the axis,
8 wherein each well comprises the parent molecule attached to a solid support;

9 b) rotating the carousel step-wise around the axis at least once,
10 each incremental step docking each of the reaction mounts at a separate station, wherein
11 (1) each station is dedicated to perform a physical step in the series during a docking,
12 wherein the physical steps include adding a liquid to a well, draining a liquid from a well,
13 and incubating; and (2) the stations are arranged to perform the series of physical steps in
14 sequence; and

15 c) performing, with each rotation of the carousel, the series of
16 physical steps in a reaction well of each of at least two of the reaction mounts, whereby a
17 chemical linkage is generated in the parent molecule.

1 20. The method of claim 19 comprising rotating the carousel a plurality
2 of times.

1 21. The method of claim 19 comprising, with at least one rotation of
2 the carousel, performing the series of steps in a reaction well of all of the reaction mounts.

1 22. The method of claim 19 wherein the series of steps is not
2 performed on a reaction well of at least one reaction mount during at least one rotation,
3 whereby the reaction mount skips the protocol during that rotation.

1 23. The method of claim 19 wherein the parent molecule is cleavable
2 from the solid support.

1 24. The method of claim 19 wherein there are 24 stations.

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- 1 25. The method of claim 19 wherein the chemical linkage links a
2 component to the parent molecule.
- 1 26. The method of claim 19 carried out in an inert atmosphere.
- 1 27. The method of claim 19 wherein the physical steps further include
2 washing a well, wherein washing comprises both adding fluid to a well and draining fluid
3 from a well at a single station.
- 1 28. The method of claim 19 wherein the steps include heating a well.
- 1 29. The method of claim 19 wherein the steps include optically
2 analyzing a well.
- 1 30. The method of claim 19 wherein the chemical linkage is selected
2 from at least one of a phosphodiester bond, a phosphorothioate bond, a phosphonate
3 bond, a phosphoramidate bond, an amide bond, an imine bond, a carbamate bond, an azo
4 bond, a sulfone bond, a sulfonide bond, a sulfonamide bond, a sulfide bond, a disulfide
5 bond, an ether bond, an ester bond, a thiourea bond, a urea bond and a carbon-carbon
6 bond.
- 1 31. The method of claim 19 wherein the chemical linkage generates a
2 new chemical linkage in the parent molecule but does not link a component to the parent
3 molecule.
- 1 32. The method of claim 25 wherein the parent molecule is a polymer
2 and the component is a monomer.
- 1 33. The method of claim 25 wherein the parent molecule is a scaffold
2 molecule and the component is an atom or molecule.
- 1 34. The method of claim 25 wherein a different fluid comprising a
2 different component is added to different wells, wherein the different fluid added to a
3 well is controlled by a programmable computer, whereby a library of different parent
4 molecules is created.
- 1 35. The method of claim 32 wherein the polymer is a nucleic acid.

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- 1 36. The method of claim 32 wherein the polymer is DNA.
- 1 37. The method of claim 32 wherein the polymer is RNA.
- 1 38. The method of claim 32 wherein the polymer is a peptide nucleic
2 acid.
- 1 39. The method of claim 32 wherein the polymer is a polypeptide.
- 1 40. The method of claim 34 wherein the computer directs the
2 generation of a library of polymers of predetermined sequence.
- 1 41. The method of claim 35 wherein the nucleic acid is coupled to a
2 solid support in the well and the series of physical steps includes, in sequence:
3 (i) washing the support;
4 (ii) dispensing a liquid comprising a deblocking agent to
5 remove the protecting group;
6 (iii) draining the liquid comprising the deblocking agent;
7 (iv) washing the support;
8 (v) dispensing a liquid comprising a coupling activator;
9 (vi) dispensing a liquid comprising a protected nucleotide;
10 (vii) draining the liquid comprising a protected nucleotide;
11 (viii) dispensing a liquid comprising a capping agent;
12 (ix) draining the liquid comprising the capping agent;
13 (x) washing the support;
14 (xi) dispensing a liquid comprising an oxidizer; and
15 (xii) draining the liquid comprising the oxidizer.
- 1 42. The method of claim 35 wherein the monomer is a modified
2 nucleotide comprising a minor groove binder.
- 1 43. The method of claim 35 comprising rotating the carousel to
2 produce a nucleic acid having between 5 and 200 nucleotides.
- 1 44. The method of claim 39 comprising rotating the carousel to
2 produce a polypeptide having between 5 and 50 amino acids.

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1 45. A method for performing in parallel a series of physical steps in a
2 chemical protocol, the method comprising the steps of:

3 a) providing a carousel that is rotatable around an axis, the carousel
4 comprising a plurality of reaction mounts, each reaction mount comprising at least one
5 reaction well arranged on a radius with respect to the axis, the radii spaced apart at equal
6 angles, whereby the wells are arranged in at least one concentric circle around the axis,
7 wherein each well comprises the parent molecule attached to a solid support;

8 b) providing a rotator that rotate the carousel step-wise around the
9 axis, each incremental step docking the reaction mounts a station, wherein: (1) each
10 station is dedicated to perform a physical step in the series during a docking and (2) the
11 stations are arranged in series from an initial station that performs an initial physical step
12 in a series of physical steps in a chemical protocol to a final station that performs a final
13 physical step in the series of physical steps;

14 c) performing an initial rotation of the carousel around the axis,
15 wherein the stations begin to perform the series of physical steps as a reaction mount
16 docks at the initial station; and

17 d) performing a final rotation of the carousel around the axis,
18 wherein the stations cease to perform the series of physical steps as a reaction mount
19 docks at the final station;

20 whereby the initial and final rotations result in one complete series
21 of steps on a reaction well of each reaction mount.

1 46. The method of claim 45 further comprising performing at least one
2 intermediate rotation between the initial and final rotations.

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